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Application No. 10/576,500

Response to Notice of Non-Compliant Amendment

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REMARKS

Remarks begin on page 7 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

- 1. (original) A modified virus ablated of its natural receptors interactions with an unmodified or non-naturally occurring cell, said modified virus comprising a non-native polypeptide, said modified virus having an altered tropism conferred by said non-native peptide, and replicating only in cells that can interact with said non-native peptide, said virus being incapable of infecting a cell through a CAR-dependent entry pathway.
- 2. (original) The modified virus of claim 1, which is derived from a virus selected from the group consisting of adenovirus, retrovirus, lentivirus, adenoassociated virus, Reoviridae, Picornaviridae, Parvoviridae, Papovaviridae and Caliciviridae.
- 3. (currently amended) The modified virus of claim 1-er-2, which is derived from human adenovirus.
- 4. (currently amended) The modified virus of any one of claims 1 to 3, which is derived from human adenovirus serotype 2 or 5.
- 5. (currently amended) The modified virus of any one of claims 1—to-4, wherein said non-native polypeptide replaces, is incorporated into, or forms a fusion protein with, a viral protein component of the wild type virus.

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- 6. (original) The modified virus of claim 5, wherein sald viral protein component is an adenoviral fiber protein.
- 7. (original) The modified virus of claim 6, wherein said non-native polypeptide is incorporated into an adenoviral fiber protein such that the wild-type fiber knob or cell binding domain thereof is removed.
- 8. (currently amended) The modified virus of any one of claims 1 to 7, wherein said non-native polypeptide is or comprises a combinatorial protein or an affibody.
- 9. (currently amended) The modified virus of any one of claims 1 to 8, wherein said non-native polypeptide comprises one or more sequence from a bacterial receptor ligand.
- 10. (currently amended) The modified virus of any-one of claims 1 to 8, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:1.
- 11. (currently amended) The modified virus of any one of claims 1—to—8, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:2.
- 12. (currently amended) The modified virus of any one of claims 1 to 11, wherein said non-native polypeptide binds a non-naturally occurring production cell or permissive cell.
- 13. (currently amended) The modified virus of any one of claims 1 to 12, further comprising a retargeting adapter comprising: i) a binding moiety for binding the non-native polypeptide and ii) a further binding molety of a receptor for retargeting said virus on cells expressing said receptor.

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- 14. (original) The modified virus of claim 13, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:1 and said binding moiety for binding the non-native polypeptide comprises at least one repeat of SEQ ID NO:2.
- 15. (original) The modified virus of claim 13, wherein said non-native polypeptide comprises at least one repeat of a sequence as set forth in SEQ ID NO:2 and said binding moiety for binding the non-native polypeptide comprises at least one repeat of SEQ ID NO:1.
- 16. (currently amended) The modified virus of any one of claims 13 to 16, wherein said adapter binds to the non-native polypeptide through non-covalent physical forces selected from the group consisting of van der waals forces, electrostatic forces, stacking interactions, hydrogen bonding and steric fit.
- 17. (currently amended) The modified virus of any-one-of-claims 1-to-12, wherein said non-native polypeptide comprises a cleavage site positioned in a location that enables a further binding moiety of a receptor to be added on the modified virus for retargeting said virus on cells expressing said receptor.
- 18. (original) The modified virus of claim 17, wherein the binding moiety is capable of binding to a cell specific ligand.
- 19. (currently amended) The modified virus of any one of claims 1 to 18, which further comprises a site for insertion of one or more desired therapeutic genes or nucleic acid molecules.
- 20. (currently amended) A cell containing a modified virus as defined in any ene of claims 1 to 19!

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- 21. (currently amended) A permissive cell for a modified virus as defined in any one of claims 1 to 19, which is capable of being cultured to propagate said modified virus.
- 22. (currently amended) A non-naturally occurring permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide as defined in any ene of claims 1-to 19.
- 23. (original) A non-naturally occurring permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide as defined in claim 10, wherein said surface receptor comprises at least one copy of the amino acid sequence as set forth in SEQ ID NO:2.
- 24. (original) A non-naturally occurring permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide as defined in claim 11, wherein said surface receptor comprises at least one copy of the amino acid sequence as set forth in SEQ ID NO:1.
- 25. (currently amended) A method for producing a modified virus as defined in any one of claims 1 to 19 in cell culture, comprising the steps of: i) genetically modifying a virus to produce a modified virus ablated of its natural receptors interactions with an unmodified or non-naturally occurring cell, said modified virus comprising a non-native polypeptide, said modified virus having an altered tropism conferred by said non-native peptide, and replicating only in cells that can interact with said non-native peptide; ii) infecting permissive cells with said modified virus; and lii) culturing said cells to produce the virus.
- 26. (original) The method of claim 25, further comprising a step of iv) harvesting the modified virus produced.
- 27. (original) The method of claim 26, further comprising a step of v) purifying the modified virus produced.

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- 28. (cancelled)
- 29. (cancelled)
- 30. (currently amended) A pharmaceutical composition comprising a modified virus as defined in any one of claims 1 to 19 and a pharmaceutically acceptable carrier or excipient.
- 31. (currently amended) A reagent kit comprising: (i) a modified virus as defined in any one of claims 1-19 and ii) a permissive cell expressing a surface receptor recognizing or binding a non-native polypeptide, said cell being capable of being infected by said modified virus as defined in any one of claims 20 to 24.
- 32. (currently amended) A medicament or a precursor thereof comprising a virus as defined in any one-of-claims 1-to-19.
- 33. (cancelled)